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EXAMINER
KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
1652	14

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/674,330	Applicant(s) HONJO ET AL.	
	Examiner Kathleen M Kerr	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-8 and 10-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s) _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

1. In response to the previous Office action (a written restriction requirement mailed on November 15, 2001, Paper No. 9), Applicants filed an election (see below). Claims 1-13 are pending in the instant application.

Election

2. Applicants' election without traverse of Group I, Claims 1-8 and 10-12 in Paper No. 10 is acknowledged. The Examiner will rejoin Group III, Claim 13, as a method of using a possibly allowable product to facilitate compact prosecution of the instant application. Thus, Claim 9 will be withdrawn from consideration, and Claims 1-8 and 10-13 will be examined herein.

Priority

3. The instant application is granted the benefit of priority for the International Application No. PCT/JP99/02283 filed on April 28, 1999 and Japanese application 10-119731 filed on April 28, 1998 as requested in the declaration. The Examiner notes that the requirements of national stage entry of the instant application had been completed within 30 months of the earliest claimed priority date; the related international application includes both a search report and a preliminary examination report.

4. Receipt is acknowledged of papers (JP 10-119731) submitted under 35 U.S.C. § 119(a)-(d), which papers have been placed of record in the file. The certified translation of said document has also been received.

Information Disclosure Statement

5. The information disclosure statement filed on October 30, 2000 (Paper No. 11) has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

Drawings

6. The drawings have been approved by the Draftsmen and are, therefore, entered as formal drawings acceptable for publication upon the identification of allowable subject matter.

Objections to the Specification

7. The specification is objected to for the numerous spelling and typographical errors, for example on page 5, line 4 "Discliption" and the numerous use of "< >" around section titles. Applicants are instructed to utilize a spelling checker program to identify all other spelling and typographical errors and make proper amendments to the specification.

8. The specification is objected to for a confusing description of the sequence listing sequences. It seems there are two disclosed isoforms of the claimed sequence, and five sequences to describe each isoform (see page 33 and page 35). Clarification of the meaning of each sequence describing the isoforms in the specification is necessary. The Examiner suggests the use of tables for a clear explanation of the sequences. Moreover, the exon discussion on page 35 is unclear; this discussion is crucial to the understanding of the isoform. Appropriate amendment to the specification is required for clarification of the sequence listing sequences.

9. The specification is objected to because on page 36, in Example 7, the BrdU incorporation assay is confusing. A definition of the abbreviation "BrdU" and a brief explanation of the assay and what it measures must be amended into the specification.

10. In the specification, the Abstract is objected to for its form and content. The word novel is redundant in a patent. The Abstract contains numerous spelling errors. No mention of the homologous A55 protein is made. It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness and correctness is essential.

11. In the specification, the Title is objected to. The word novel is redundant in a patent title.

Objections to the Claims

12. Claims 6-8 are objected to under 37 C.F.R. § 1.75(c) as being in improper form because a multiple dependent claim 6. See M.P.E.P. § 608.01(n). Claim 6 should read "according to any one of claims 3-5". The claims will be examined as if this correction has been made.

13. Claim 8 is objected to under 37 C.F.R. § 1.75(c) as being in improper form because a multiple dependent claim 8. See M.P.E.P. § 608.01(n). Claim 8 depends from more than one claim not in the alternative. The Examiner suggests amending the claim language to depend only from Claim 7 while remaining clear that the polypeptide is that which is encoded by the cDNA on the vector in the host cell.

14. Claim 10 is objected to for containing non-elected subject matter. The phrase "or the antibody according to claim 9" must be deleted. The claims will be examined as if this correction has been made.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1-8 and 10-13 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claims 1, 4, and 5, the phrase "that comprising" is confusing. The word ---that---should be deleted from the phrase in each case.

16. Claims 1, 3, 5-8, and 10-13 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 1, the term "homologue" is unclear. Is this a structural homologue? If so, what degree of sequence identity renders another product a homologue? Is this a functional homologue? If so, what function is intended? Appropriate clarification is required.

17. Claims 2, 8, and 10-13 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 2, the phrase "consists (comprising)" is confusing.

These terms have very distinct and different definitions. The term "consists of" indicates to the end of the sequence and nothing else while the term "comprising" indicates the exact sequence in addition to other sequence that might be connected. Thus, the scope is very different based on the two different definitions. Since "comprising" is the broader term, the claims will be examined as if this definition is intended. Appropriate clarification is required.

18. Claims 6-8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 6, the term "carrying" is not a term of art. The more appropriate term is ---comprising---.

19. Claim 13 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claim is a method claim specifying no method steps. Also, in line 2, "the said" is redundant and should be either "the" or "said" since these terms are both used to identify the antecedent of the polypeptide.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

20. Claims 1, 3-8 and 10-13 are rejected under 35 U.S.C. 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to products, such as DNA and polypeptides, wherein the structure and function is not particularly defined. Claim 1 is drawn to *any* polypeptide with *any* amount of sequence relatedness to SEQ ID NOs:3, 4, 8, or 9; this variation comes from the broad terms "homologue", "fragment", and "homologue of the fragment". In Claims 4 and 5, this variation comes from the term "fragment ... selectively hybridized". Claim 2 is omitted from this rejection because there is no variation in the sequence, and this defined sequence has a defined, albeit loosely, function.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

The instant specification discloses polynucleotides encoding polypeptides having particular sequence identity with SEQ ID NOs: 3, 4, 8, or 9. Applicants may have fully

described the genus relating to said SEQ ID NOs with both sequence identity limitations and functional limitations (encoding an A55 polypeptide homologue does not appear to be a particular function). However, the genus of the instant claims also contains polynucleotides within the sequence identity limitations, but having different function. Applicants have not fully described a genus that has sequence identity limitations in the absence of functional limitations.

21. Claims 1-8 and 10-13 are rejected under 35 U.S.C. § 112, first paragraph, enablement, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The invention is drawn to mouse A55 polypeptides, encoding cDNAs, and the like. One of skill in the art would be required to perform undue experimentation to use the claimed invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or

absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Mouse A55 is disclosed as a glycosylated, secreted protein having EGF-like domains (see page 34 and page 36 of the specification). Applicants identify A55 as having "functions to suppress smooth muscle cells" (see page 4 of the specification) by virtue of the ability of A55 to suppress cell proliferation/viability in cultured rat aorta cells (see Figure 1 and Example 7). Firstly, the error in this data is large for such a small effect. Secondly, no control concerning the interaction of BrdU and A55 is reported. The systems and pathways of suppression of cell proliferation are highly complex. The particular function of the A55 protein is wholly unpredictable even if the results of Figure 1 can be supported through proper control experiments. Additionally, these experiments are in cultured cells; the nexus between cultured cells and *in vivo* results is highly limiting. Thus, it is not clear to one of skill in the art what function, if any A55 polypeptide has. The EGF-like domains could serve to interact with any one or more of the numerous EGF-like proteins in mammalian cells. One would then be required to assay for functionality, which assays are wholly unpredictable. The specification presents no guidance or working examples for such experimentation.

22. Claims 10-12 are rejected under 35 U.S.C. § 112, first paragraph, enablement, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant claims are drawn to "pharmaceutical compositions"

comprising the disclosed polypeptide. For such compositions to be "pharmaceutical" in nature, therapeutic use must be enabled. In the absence of a disclosed effective therapeutic use, undue experimentation would be required to produce a pharmaceutical composition.

The factors to be considered in determining whether undue experimentation is required are summarized above.

No guidance or working examples of the A55 polypeptide as an effective therapeutic are disclosed. While abnormal proliferation of smooth muscle is implicated in many disease states (see page 13 of the instant specification), no effective treatments using A55 polypeptides as therapeutics are disclosed. The nature of the invention is such that extensive and unpredictable experimentation is required to determine if A55 polypeptides can be useful as therapeutics. Thus, the instant claims, drawn to pharmaceutical compositions, are not enabled. The Examiner suggests the deletion of the term "pharmaceutical".

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

23. Claims 1-8 and 10-13 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility. To fulfill the utility requirement of 35 U.S.C. § 101, an invention must have a specific, substantial, and credible utility that is disclosed in the specification or that is well established as considered by one of ordinary skill in the art.

The specification expounds greatly on the utility of the instant invention (see pages 13-28). However, all these utilities are speculative and lack specificity due to the fact that the

function of A55 is unclear. Particularly, the specification speculates that A55 may be useful in the treatment of diseases characterized by abnormal proliferation of smooth muscle cells (see page 13). However, aorta mouse cells in culture are an unproven model for *all* smooth muscle cells, *in vivo*, and *any* treatable organism. The remaining speculations are a list from EGF-like family activities and are wholly unidentified in the specification or the art.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. § 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. § 122(b). Therefore, this application is examined under 35 U.S.C. § 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. § 102(e)).

24. Claims 3-5 are rejected under 35 U.S.C. § 102(b) as being anticipated by **Lee *et al.*** ("EST190962 Normalized rat spleen, Bento Soares Rattus sp. cDNA clone RSPAA89 5` end, mRNA sequence." GenBank Accession Number AA801465 created on July 19, 1995). The instant claims are drawn to cDNAs that encode fragments and/or homologues of SEQ ID NOs: 3 or 8 and are drawn to cDNAs that selectively hybridize to SEQ ID NOs: 2 or 7. Since the two

isoforms disclosed are cDNA SEQ ID NOs: 2 and 7 and their encoded, full-length proteins are SEQ ID NOs: 3 and 8, only these SEQ ID NOs will be referenced in the instant rejection; the rejection is not based on an *exact* match between the art and any of the full-length disclosed sequences.

Lee *et al.* teach a polynucleotide sequence that encodes a protein that is 95% identical to SEQ ID NO:8 from residue 297 to residue 443; the protein of Lee *et al.* is, thus, a fragment homologue of SEQ ID NO:8. Moreover, the sequence of Lee *et al.* is highly similar to SEQ ID NOs:2 and 7, which are identical in this region, and will selectively hybridize to SEQ ID NOs:2 and 7.

25. Claims 1, 3-8 and 10-13 are rejected under 35 U.S.C. § 102(e) as being anticipated by Bandman *et al.* (USPN 5,872,234 published on February 16, 1999 and filed on June 27, 1997). The instant claims are drawn to polypeptide fragments and/or homologues related to SEQ ID NOs: 3 and 8. The instant claims are also drawn to cDNA fragments that selectively hybridize to SEQ ID NOs: 2 and 7 or that selectively hybridize to a DNA that encodes SEQ ID NOs: 3 and 8. Since the two isoforms disclosed are cDNA SEQ ID NOs: 2 and 7 and their encoded, full-length proteins are SEQ ID NOs: 3 and 8, only these SEQ ID NOs will be referenced in the instant rejection; the rejection is not based on an *exact* match between the art and any of the disclosed sequences. The instant claims are also drawn to vectors, host cells, methods of making polypeptides, pharmaceutical compositions, and methods of screening for antagonists related to the noted sequence above.

Bandman *et al.* teach an isolated human ECMP polypeptide (sequence 1 in sequence listing) that is 91% identical to SEQ ID NOs: 3 and 8 (see attached alignments); the protein of

Bandman *et al.* is, thus, a fragment homologue of SEQ ID NOs: 3 and 8. Bandman *et al.* also teach the encoding DNA sequence (sequence 2 in sequence listing) that is greater than 79% identical to SEQ ID NO:7 and greater than 66% identical to SEQ ID NO:2 (see attached alignments); the DNA sequence of Bandman *et al.* will selectively hybridize to SEQ ID NOs:2 and 7. Bandman *et al.* also teach their polypeptides in pharmaceutical compositions and their DNA in vectors, in host cells, and in methods of making polypeptides (see Columns 2-3). Bandman *et al.* also teach the polypeptides in methods of screening for agents which specifically bind the polypeptide (see Column 21, lines 15-17).

26. Claims 3-5 are rejected under 35 U.S.C. § 102(a) as being anticipated by **Marra *et al.*** ("ve31a08.r1 Ko mouse embryo 11 5dpc Mus musculus cDNA clone IMAGE:819734 5' similar to TR:G458228 G458228 EXTRACELLULAR PROTEIN PRECURSOR, mRNA sequence." GenBank Accession Number AA437518 created on May 30, 1997). The instant claims are drawn to cDNAs that encode fragments and/or homologues of SEQ ID NOs: 3 or 8 and are drawn to cDNAs that selectively hybridize to SEQ ID NOs: 2 or 7. Since the two isoforms disclosed are cDNA SEQ ID NOs: 2 and 7 and their encoded, full-length proteins are SEQ ID NOs: 3 and 8, only these SEQ ID NOs will be referenced in the instant rejection.

Marra *et al.* teach a mouse polynucleotide sequence identical to SEQ ID NO:2 from 1130bp-1429bp (see attached alignment) and to SEQ ID NO:7 from 1326bp-1625bp; this sequence encodes approximately 100 amino acids at the C-terminus of the A55 polypeptide (SEQ ID NOs: 3 or 8) exactly.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

27. Claims 1 and 6-8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over **Lee *et al.*** ("EST190962 Normalized rat spleen, Bento Soares Rattus sp. cDNA clone RSPAA89 5' end, mRNA sequence." GenBank Accession Number AA801465 created on July 19, 1995) in view of **Bork *et al.*** (From genome sequences to protein function. Current Opinion in Structural Biology (1994) 4:393-403). The instant claims are drawn to polypeptide fragments and/or homologues of SEQ ID NOs: 3 or 8, vectors and host cells comprising DNA and/or DNA fragments that selectively hybridize to SEQ ID NOs: 2 or 7, and methods of making said polypeptide fragments. Since the two isoforms disclosed are cDNA SEQ ID NOs: 2 and 7 and their encoded, full-length proteins are SEQ ID NOs: 3 and 8, only these SEQ ID NOs will be referenced in the instant rejection; the rejection is not based on an *exact* match between the art and any of the disclosed sequences.

Lee *et al.* teach as described above. Lee *et al.* do not teach the encoded protein of the EST. Nor do Lee *et al.* teach methods of identifying a full-length gene and producing its protein product.

Bork *et al.* teach the technologies of taking small portions of genes (ESTs) and producing the protein products (see Abstract and page 394, left column). Such technologies require the use of vectors and host cells as claims in Claims 6-8.

It would have been obvious to one of ordinary skill in the art to (2) screen a rat cDNA library for the full-length gene of the EST taught by Lee *et al.*, (2) comprise a vector containing said full-length gene, and (3) express said full-length gene in a host cell to make the encoded protein because the sequence of Lee *et al.* is taught as an EST and ESTs are expressed sequence tags of full-length proteins being expressed, in this case, in rat. Expressed proteins are useful to the structure and/or function of organisms. One would have been motivated to combine the instant prior art because, while the prediction of protein function from ESTs is becoming more commonplace and predictable, much information must be confirmed and/or learned from assaying the expressed protein product of an EST. One would have had a reasonable expectation of success that the EST taught be Lee *et al.* could identify the full-length gene because said EST is a large portion of the full-length protein. The cloning of such genes and their expression is also reasonably within the skills of an artisan at the time of the invention.

The Examiner notes that the claims to the exact protein sequence, Claim 2, cannot be anticipated or obviated by the instant prior art because portions of the full length sequence, while possibly able to identify the gene encoding the full-length protein claimed, cannot predict the structure of the full-length sequence (*In re* Deuel). Claims drawn to the full-length DNA sequences would also not be anticipated or obviated by this prior art; however, no such claims are claimed presently since the cDNA claims contain hybridizing language.

28. Claims 1 6-8 and 10-12 are rejected under 35 U.S.C. § 103(a) as being unpatentable over **Marra *et al.*** ("ve31a08.r1 Ko mouse embryo 11 5dpc Mus musculus cDNA clone IMAGE:819734 5' similar to TR:G458228 G458228 EXTRACELLULAR PROTEIN PRECURSOR, mRNA sequence." GenBank Accession Number AA437518 created on May 30,

1997) in view of **Bork *et al.*** (From genome sequences to protein function. Current Opinion in Structural Biology (1994) 4:393-403). The instant claims are drawn to polypeptide fragments and/or homologues of SEQ ID NOs: 3 or 8, vectors and host cells comprising DNA and/or DNA fragments that selectively hybridize to SEQ ID NOs: 2 or 7, and methods of making said polypeptide fragments. Since the two isoforms disclosed are cDNA SEQ ID NOs: 2 and 7 and their encoded, full-length proteins are SEQ ID NOs: 3 and 8, only these SEQ ID NOs will be referenced in the instant rejection.

Marra *et al.* teach as described above. Marra *et al.* do not teach the encoded protein of the EST. Nor do Marra *et al.* teach methods of identifying a full-length gene and producing its protein product.

Bork *et al.* teach the technologies of taking small portions of genes (ESTs) and producing the protein products (see Abstract and page 394, left column). Such technologies require the use of vectors and host cells as claims in Claims 6-8.

It would have been obvious to one of ordinary skill in the art to (2) screen a mouse cDNA library for the full-length gene of the EST taught by Marra *et al.*, (2) comprise a vector containing said full-length gene, and (3) express said full-length gene in a host cell to make the encoded protein because the sequence of Marra *et al.* is taught as an EST and ESTs are expressed sequence tags of full-length proteins being expressed, in this case, in mouse. Expressed proteins are useful to the structure and/or function of organisms. One would have been motivated to combine the instant prior art because, while the prediction of protein function from ESTs is becoming more commonplace and predictable, much information must be confirmed and/or learned from assaying the expressed protein product of an EST. One would have had a

reasonable expectation of success that the EST taught be Marra *et al.* could identify the full-length gene because said EST is a large portion of the full-length protein. The cloning of such genes and their expression is also reasonably within the skills of an artisan at the time of the invention.

The Examiner notes that the claims to the exact protein sequence, Claim 2, cannot be anticipated or obviated by the instant prior art because portions of the full length sequence, while possibly able to identify the gene encoding the full-length protein claimed, cannot predict the structure of the full-length sequence (*In re* Deuel). Claims drawn to the full-length DNA sequences would also not be anticipated or obviated by this prior art; however, no such claims are claimed presently since the cDNA claims contain hybridizing language.

Conclusion

29. Claims 1-8 and 10-13 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK
January 24, 2002